REMARKS

Claims 4, 6-8, 10-17 and 19-21 were pending in the present application. Claims 17 and 19-21 were rejected. Claims 16, 17, 19 and 20 are herein amended. New claims 22-39 are added herein. Claims 1-15 and 18 are herein cancelled without prejudice. No new matter has been added. Applicants thank the Examiner for the courtesies extended in the telephone interview of February 18, 2009. Applicants' Statement of the Substance of the Interview is incorporated herein.

Applicants' Response to Claim Rejections under 35 U.S.C. §112

Claims 17 and 19-21 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is the position of the Office Action that claim 17 is indefinite because the preamble of claim 17 recites a method of screening a candidate compound in test samples, but the claim does not set forth steps with respect to how to screen a candidate compound and how to select a candidate compound.

It appears that this alleged indefiniteness is in part due to the fact that the preamble recites "a candidate compound in test samples," but the steps in the body of the claim recite "test samples" and "a test sample." In other words, the body of the claim does not recite "a candidate compound."

Therefore, Applicants herein amend claim 17 in order to improve its clarity and form. In particular, Applicants herein amend the claims to recite a method of screening for "a candidate compound" that is an agonist of the receptor p2y9. Applicants herein amend claim 17 in order to clarify the steps of the method. Part (a) is clarified to recite that two groups of cells are prepared. Steps (b) and (c) are amended to clarify the addition of LPA, and the monitoring of associated intracellular activity (calcium concentration and cAMP concentration). Steps (d) and (e) are amended to clarify the addition of the candidate compound and the monitoring of the same associated intracellular activity (calcium concentration and cAMP concentration). Steps (f) and (g) are amended to clarify that the determination that the candidate compound is an agonist depends on the comparison of the intracellular activity. Furthermore, Applicants herein amend claim 17 in order to move the phrase "wherein said G protein-coupled p2y9 protein comprises an amino acid sequence having a sequence identity of at least 95% to the amino acid sequence of SEQ ID NO: 1" from the preamble of the claim to the body of the claim. Please see amended claim 17.

Similarly, Applicants herein add new claim 22. In particular, new claim 22 recites a method of screening for "a candidate compound" that is an antagonist of the receptor p2y9. Part (a) recites that two groups of cells are prepared. Steps (b) and (c) recite the addition of LPA, and the monitoring of associated intracellular activity (calcium concentration and cAMP concentration). Steps (d) and (e) recite the addition of the candidate compound and LPA, and the monitoring of the same associated intracellular activity (calcium concentration and cAMP concentration). Steps (f) and (g) recite that the determination that the candidate compound is an

antagonist depends on the comparison of the intracellular activity. Please see new claim 22. This subject matter is supported at least by paragraph [0001].

Additionally, Applicants herein amend claim 16 to improve its clarity and form. Claim 16 previously recited "G protein-coupled p2y9s." Although the specification refers to "p2y9s" in several places, this is an obvious error. Applicants herein amend claim 16 and specification in order to correct this error. A similar correction is made to the term "p2y5s." Additionally, Applicants herein amend claim 16 to improve its clarity. Please see amended claim 16. Furthermore, Applicants respectfully submit that claim 16 shares a "special technical feature" with claims 17 and 22 and thus should be examined in the present application.

Furthermore, Applicants herein add new claim 34, which recites a method of screening for a compound that acts as an inhibitor of binding of LPA to G protein-coupled receptor p2y9. Please see new claim 34. This subject matter is supported at least by Figure 25 and Example 9 in the specification. Applicants respectfully submit that claim 34 shares a "special technical feature" with claims 17 and 22 and thus should be examined in the present application.

Claims 17 and 19-21 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

It is the position of the Office Action that the specification does not provide sufficient support for the genus of p2y9 variants. The Office Action states that the claims do not require that the p2y9 proteins possess any particular conserved structure or biological functions.

In the telephone interview of February 18, 2009, Applicants discussed whether claims reciting a protein having 95% homology with respect to SEQ ID NO: 1 would allowable. The Examiner indicated that if the claims were amended to recite "wherein said G protein-coupled receptor p2y9 comprises seven transmembrane regions," the written description rejection would be withdrawn.

However, the Examiner further stated that absent evidence to show that some specific structural feature gives rise to a specific biological function, the an enablement rejection would likely be raised. The Examiner indicated that this could be demonstrated by a showing that the homologs in the Alignment No. 1 (previously filed) and Alignment No. 3 (submitted herewith) bind LPA. Human sequence Acc. No. Q99577 is identical to SEQ ID NO: 1. Thus, the specification supports binding of this protein to LPA. However, Applicants herewith submit evidence to show that Acc. No. AK045289 (mouse) will bind LPA. Acc. No. AK045289 is mouse p2y9, also known as GPR23. The amino acid sequence of GPR23 is 98.1% homologous to SEQ ID NO: 1. The attached data shows (A) the binding amount of radiolabeled LPA increased with the concentration increase against mouse GPR23-transiently-developed RH7777 cell membranes, and (B) that the Bound/Free (B/F) ratio constantly decreases with the increase in labelled LPA. Thus, the binding activity is show by an ordinary receptor-coupling experiment. Please see the attached Declaration under 37 CFR 1.132. Thus, Applicants respectfully submit that it is clear that allele variants having at least 95% homology to human p2y9 will have similar LPA receptor activity.

Furthermore, as the Office Action indicates, "seven transmembrane regions" does not necessarily confer peculiar binding to LPA. However, a G-protein coupled receptor having seven transmembrane regions is firmly fixed to the cell membrane and forms a ligand binding domain outside the cell, which establishes the structure which peculiarly binds to its corresponding ligand. Please see the attached excerpt from *Molecular Biology of the Cell*, Third Edition.

Furthermore, Applicants herewith submit a copy of Joost and Methner. This document indicates G-protein coupled receptors are classified in the same class based on their sequence similarity in the evolutionary tree. This document further indicates indicate that even different receptors generally recognized similar ligands if they are closely related in the evolutionary tree. As such, allele receptors with at least 95% homology will recognize the same ligand. This document also indicates that most of G-protein coupled receptors are orphan receptors, which do not have determined specific ligands.

In view of the above, Applicants respectfully submit that the claims reciting at least 95% homology to SEQ ID NO: 1 fully comply with all requirements of 35 U.S.C. §112. However, in order to further expedite examination, Applicants also add new claims 26 and 30, which recite exactly the sequence of SEQ ID NO: 1. Favorable reconsideration is respectfully requested.

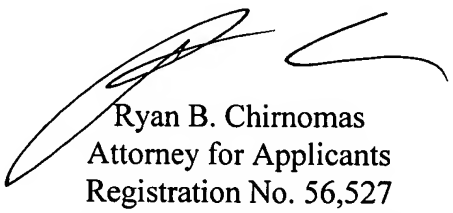
For at least the foregoing reasons, the claimed invention distinguishes over the cited art and defines patentable subject matter. Favorable reconsideration is earnestly solicited.

Should the Examiner deem that any further action by applicants would be desirable to place the application in condition for allowance, the Examiner is encouraged to telephone applicants' undersigned attorney.

If this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. The fees for such an extension or any other fees that may be due with respect to this paper may be charged to Deposit Account No. 50-2866.

Respectfully submitted,

WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP



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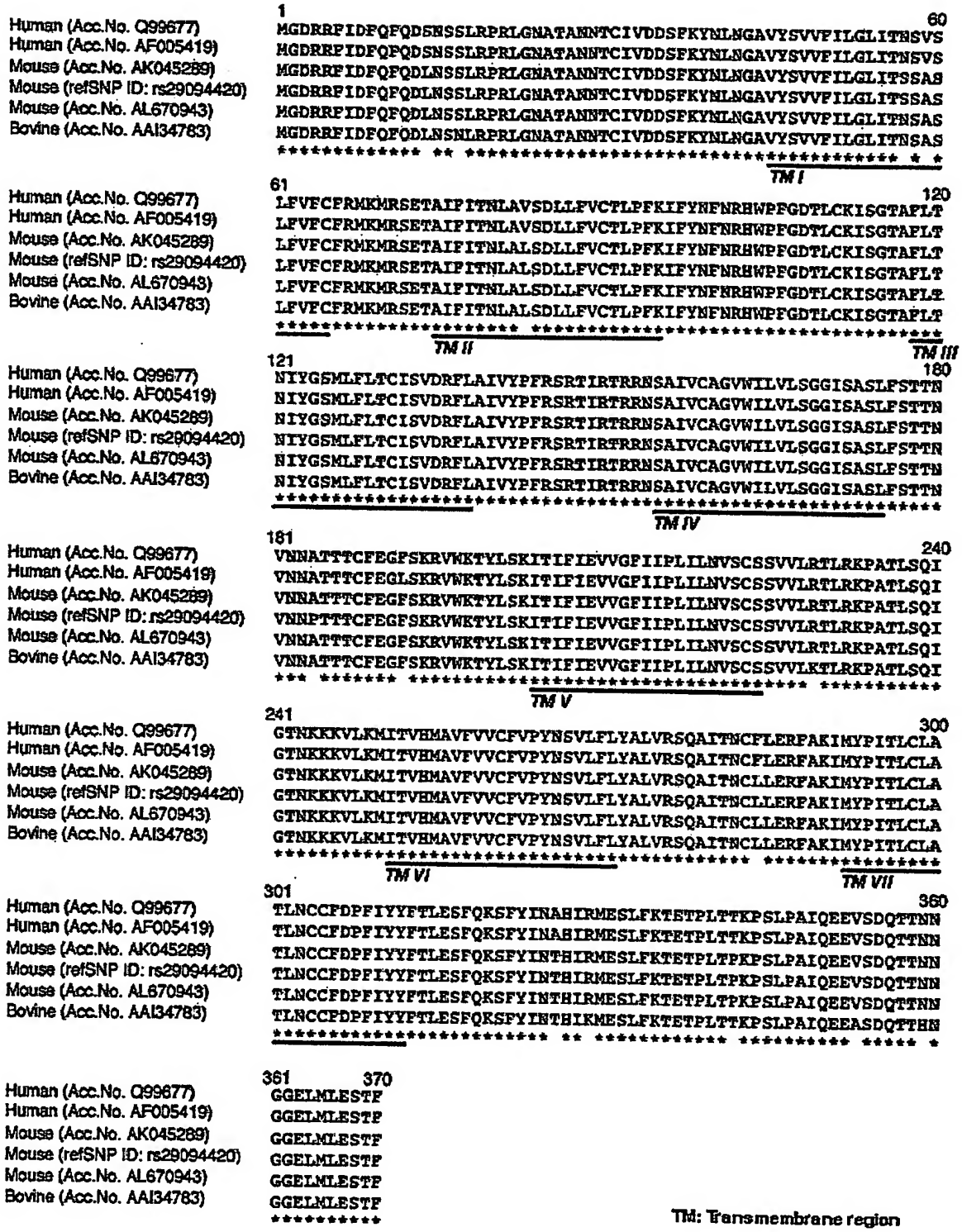
Enclosures:
(1) Alignment No. 3
(2) Declaration under 37 CFR §1.132
(3) Excerpt from *Molecular Biology of the Cell*, Third edition (pages 734-735)
(4) Joost, P and Methner A. "Phylogenetic analysis of 277 human G-protein-coupled receptors as a tool for the prediction of orphan receptor ligands." *Genome Biology*, 3: 11 (2002).



TM: Transmembrane region